

## Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application.

### Listing of Claims:

Claim 1 (Currently amended): A method for modeling cellular metabolism of an organism, comprising:

constructing a flux balance analysis model utilizing stoichiometric mass balances of metabolic

and cellular composition information to identify boundaries for available flux

distributions of a metabolic network; and

applying logic constraints to the flux balance analysis model ~~to thereby tighten the boundaries~~

~~for the available flux distributions~~ to produce an altered flux balance analysis model, wherein

said logic constraints constrain a boundary for an available flux distribution to thereby

improve predictive capabilities of said flux balance analysis model.

Claim 2 (Previously presented): The method of claim 1 wherein at least a subset of the logic constraints are capable of protecting against violation of a kinetic barrier.

Claim 3 (Previously presented): The method of claim 1 wherein the logic constraints further include a set of connectivity restraints.

Claim 4 (Currently amended): The method of claim 1 further comprising the step of applying mixed-integer linear programming to said flux balance analysis model having improved predictive capabilities to solve for a desired metabolic outcome.

Claim 5 (Original): The method of claim 1 further comprising the step of solving for a desired metabolic outcome.

Claim 6 (Currently amended): A method for modeling cellular metabolism of an organism that improves upon a flux balance analysis model, comprising:

constructing the flux balance analysis model utilizing stoichiometric mass balances of metabolic

and cellular composition information to identify boundaries for available flux

distributions of a metabolic network; and

applying a plurality of logic constraints to the flux balance analysis model to ~~thereby tighten the~~

~~boundaries for the available flux distributions~~ produce an altered flux balance analysis

model, wherein said plurality of logic constraints constrain a boundary for available flux

distributions to thereby improve predictive capabilities of said flux balance analysis

model.

Claim 7 (Currently amended): The method of claim 6, further comprising selecting the set of logic constraints to protect against violation of a kinetic or regulatory barrier.

Claim 8 (Original): The method of claim 6 wherein the logic constraints are defined by a relationship between changes in reaction fluxes and metabolic concentrations.

Claim 9 (Cancelled).

Claim 10 (Original): The method of claim 6 wherein the logic constraints are represented by binary variables.

Claim 11 (Original): The method of claim 10 wherein a first binary variable represents the presence of a reaction and a second binary variable represents the absence of a reaction.

Claim 12 (Original): The method of claim 6 further comprising applying a computational procedure to identify a minimal set of metabolic reactions.

Claim 13 (Original): The method of claim 12 further comprising selecting a growth rate, and wherein the step of applying a computational procedure is applying a computational procedure to identify the minimal set of metabolic reactions capable of supporting the growth rate.

Claim 14 (Currently amended): The method of claim 6 further comprising the step of applying mixed-integer linear programming to said flux balance analysis model having improved predictive capabilities to solve for a desired metabolic outcome.

Claim 15 (Previously presented): The method of claim 6 further comprising the step of solving for a desired metabolic outcome.

Claim 16 (Currently amended): The method of claim 15 further comprising engineering ~~the~~ a change in an organism based on the desired metabolic outcome.

Claims 17-18 (Cancelled).

Claim 19 (Currently amended): A system for modeling cellular metabolism of an organism, comprising:

a flux balance analysis model contained on a computer readable medium utilizing stoichiometric mass balances of ~~the~~ metabolic and cellular composition information to identify boundaries for available flux distributions of a metabolic network;

a plurality of logic constraints applied to the flux balance analysis model ~~to tighten the boundaries for available flux distributions~~, the logic constraints selected from the set consisting of qualitative kinetic information constraints, qualitative regulatory information constraints, and differential DNA microarray experimental data constraints; and

commands for producing an altered flux balance analysis model wherein said plurality of logic constraints constrain a boundary for available flux distributions to thereby improve predictive capabilities of said flux balance analysis model.

Claim 20 (Previously presented): The method of claim 1 wherein the logic constraints further include qualitative regulatory information constraints.

Claim 21 (Currently amended): The ~~method~~ system of claim 20 wherein at least a subset of the logic constraints protect against violation of a regulatory barrier.

Claim 22 (Currently amended): The ~~system~~method of claim 1 wherein the logic constraints further include DNA experimental data constraints.

Claim 23 (Currently amended): A method for modeling cellular metabolism of an organism, comprising:

constructing a flux balance analysis model of a metabolic network;

applying constraints to the flux balance analysis model, wherein the constraints include

qualitative kinetic information constraints, qualitative regulatory information constraints,  
~~and differential DNA microarray experimental data constraints, or a combination thereof;~~  
and

producing an altered flux balance analysis model wherein said constraints constrain a boundary  
for an available flux distribution to thereby improve predictive capabilities of said flux  
balance analysis model.

Claim 24 (Previously presented): The method of claim 23 wherein the constraints include logic constraints to protect against violation of a regulatory barrier.

Claim 25 (Previously presented): The method of claim 23 wherein the constraints further include connectivity restraints.

Claim 26 (Currently amended): The method of claim 23 further comprising applying mixed-integer linear programming to said flux balance analysis model having improved  
predictive capabilities to solve for a desired metabolic outcome.

Claim 27 (Previously presented): The method of claim 23 further comprising solving for a desired metabolic outcome.

Claims 28-29 (Cancelled).

Claim 30 (Currently amended): A method for modeling cellular metabolism of an organism that improves upon a flux balance analysis model, comprising:

constructing the flux balance analysis model utilizing stoichiometric mass balances of metabolic and cellular composition information to identify boundaries for available flux distributions of a metabolic network;

applying a plurality of logic constraints to the flux balance analysis model to ~~tighten the boundaries~~ produce an altered flux balance analysis model, wherein said plurality of logic constraints constrain a boundary for available flux distributions to thereby improve predictive capabilities of said flux balance analysis model; and

applying mixed-integer linear programming to said flux balance analysis model having improved predictive capabilities to solve for a desired metabolic outcome associated with of the flux balance analysis model of the organism.

Claim 31 (Previously presented): The method of claim 30 further comprising the step of solving for the desired metabolic outcome.

Claim 32 (Previously presented): The method of claim 31 further comprising engineering a change in the organism based on the desired metabolic outcome.

Claim 33 (Currently amended): A method for modeling cellular metabolism of an organism, comprising:

constructing a flux balance analysis model using stoichiometric mass balances of metabolic and cellular composition information to identify stoichiometric boundaries for available flux distributions of a metabolic network;

determining logic constraints to apply to the flux balance analysis model ~~to tighten the stoichiometric boundaries~~, the logic constraints based on qualitative relationships between changes in reaction fluxes and changes in metabolite concentrations; and

applying the logic constraints to the flux balance analysis model ~~to thereby tighten the stoichiometric boundaries~~ produce an altered flux balance analysis model, wherein said logic constraints constrain a boundary for an available flux distribution to thereby improve predictive capabilities of said flux balance analysis model.